

wherein

ack
R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R² is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R³ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic;

R⁵ is $-(CH_2)_x-Ar-R^{5'}$ where R^{5'} is selected from the group consisting of $-O-Z-NR^8R^{8'}$ and $-O-Z-R^{12}$ wherein R⁸ and R^{8'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R⁸ and R^{8'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of $-C(O)-$ and $-SO_2-$,

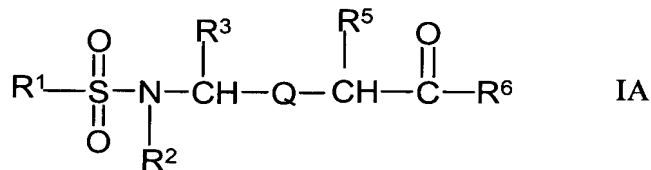
Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

x is an integer of from 1 to 4;

Q is $-C(X)NR^7-$ wherein R⁷ is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur; and pharmaceutically acceptable salts thereof.

Please add new claims 35-59 as follows:

35. A compound of formula IA:



09987619-11501
FOSTT-6T6660
wherein

R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R² is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R³ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic;

R⁵ is -(CH₂)_x-Ar-R^{5'} and R^{5'} is selected from the group consisting of -O-Z-NR⁸R^{8'} and -O-Z-R¹² wherein R⁸ and R^{8'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R⁸ and R^{8'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-,

Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

x is an integer of from 1 to 4;

Q
2
cont

R⁶ is selected from the group consisting of amino, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, -O-(N-succinimidyl), -NH-adamantyl, -O-cholest-5-en-3- β -yl, -NHOY where Y is hydrogen, alkyl, substituted alkyl, aryl, and substituted aryl, -NH(CH₂)_pCOOY where *p* is an integer of from 1 to 8 and Y is as defined above, -OCH₂NR⁹R¹⁰ where R⁹ is selected from the group consisting of -C(O)-aryl and -C(O)-substituted aryl and R¹⁰ is selected from the group consisting of hydrogen and -CH₂COOR¹¹ where R¹¹ is alkyl, and -NHSO₂Z' where Z' is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Q is -C(X)NR⁷- wherein R⁷ is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur;
and pharmaceutically acceptable salts thereof.

36. A compound according to Claims 1 or 35 wherein R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl.

37. A compound according to Claims 1 or 35 wherein R¹ is selected from the group consisting of methyl, isopropyl, *n*-butyl, benzyl, phenethyl, phenyl, 4-methylphenyl, 4-*t*-butylphenyl, 2,4,6-trimethylphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,4-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 3-chloro-4-fluorophenyl, 4-bromophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 4-*t*-butoxyphenyl, 4-(3'-dimethylamino-*n*-propoxy)-phenyl, 2-carboxyphenyl, 2-(methoxycarbonyl)phenyl, 4-(H₂NC(O)-)phenyl, 4-(H₂NC(S)-)phenyl, 4-cyanophenyl, 4-trifluoromethylphenyl, 4-trifluoromethoxyphenyl, 3,5-di-(trifluoromethyl)phenyl, 4-nitrophenyl, 4-aminophenyl, 4-(CH₃C(O)NH-)phenyl, 4-(PhNHC(O)NH-)phenyl, 4-amidinophenyl, 4-methylamidinophenyl, 4-(CH₃SC(=NH)-)phenyl, 4-chloro-3-(H₂NS(O)₂-)phenyl, 1-naphthyl, 2-naphthyl, pyridin-2-yl, pyridin-3-yl,

pyrimidin-2-yl, quinolin-8-yl, 2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl, morpholin-4-yl, 2-thienyl, 5-chloro-2-thienyl, 2,5-dichloro-4-thienyl, 1-N-methylimidazol-4-yl, 1-N-methylpyrazol-3-yl, 1-N-methylpyrazol-4-yl, 1-N-butylpyrazol-4-yl, 1-N-methyl-3-methyl-5-chloropyrazol-4-yl, 1-N-methyl-5-methyl-3-chloropyrazol-4-yl, 2-thiazolyl and 5-methyl-1,3,4-thiadiazol-2-yl.

38. A compound according to Claims 1 or 35 wherein R² is selected from the group consisting of hydrogen, methyl, phenyl, benzyl, -(CH₂)₂-2-thienyl, and -(CH₂)₂-φ.

39. A compound according to Claims 1 or 35 wherein R³ is selected from the group consisting of methyl, phenyl, benzyl, diphenylmethyl, -CH₂CH₂-COOH, -CH₂-COOH, 2-amidoethyl, *iso*-butyl, *t*-butyl, -CH₂O-benzyl and hydroxymethyl.

40. A compound according to Claims 1 or 35 wherein Q is -C(O)NH- or -C(S)NH-.

41. A compound according to Claims 1 or 35 wherein Ar is aryl or substituted aryl.

42. A compound according to Claim 41 wherein Ar is phenyl or substituted phenyl and x is 1.

43. A compound according to Claim 1 or 35 wherein R⁵ is selected from the group consisting of

- 3-[(CH₃)₂NC(O)O-]benzyl,
- 4-[(CH₃)₂NC(O)O-]benzyl,
- 4-[(CH₃)₂NS(O)₂O-]benzyl,
- 4-[(piperidin-1'-yl)C(O)O-]benzyl,
- 4-[(piperidin-4'-yl)C(O)O-]benzyl,

[illegible]

4-[(1'-methylpiperidin-4'-yl)C(O)O-]benzyl,
4-[(4'-hydroxypiperidin-1'-yl)C(O)O-]benzyl,
4-[(4'-formyloxypiperidin-1'-yl)C(O)O-]benzyl,
4-[(4'-ethoxycarbonylpiperidin-1'-yl)C(O)O-]benzyl,
4-[(4'-carboxylpiperidin-1'-yl)C(O)O-]benzyl,
4-[(3'-hydroxymethylpiperidin-1'-yl)C(O)O-]benzyl,
4-[(4'-hydroxymethylpiperidin-1'-yl)C(O)O-]benzyl,
4-[(4'-phenyl-1'-Boc-piperidin-4'-yl)-C(O)O-]benzyl,
4-[(4'-piperidon-1'-yl ethylene ketal)C(O)O-]benzyl,
4-[(piperazin-4'-yl)-C(O)O-]benzyl,
4-[(1'-Boc-piperazin-4'-yl)-C(O)O-]benzyl,
4-[(4'-methylpiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-methylhomopiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(2-hydroxyethyl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-phenylpiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(4-trifluoromethylpyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyrimidin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-acetyl piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyridin-4-ylC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylNHC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylNHC(S)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-methanesulfonylpiperazin-1'-yl)-C(O)O-]benzyl,
4-[(4'-trifluoromethanesulfonylpiperazin-1'-yl)-C(O)O-]benzyl,
4-[(morpholin-4'-yl)C(O)O-]benzyl,
3-nitro-4-[(morpholin-4'-yl)-C(O)O-]benzyl,
4-[(thiomorpholin-4'-yl)C(O)O-]benzyl,
4-[(thiomorpholin-4'-yl sulfone)-C(O)O-]benzyl,

4-[(pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-methylpyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(methoxycarbonyl)pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(hydroxymethyl)pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(N,N-dimethylamino)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(2'-(N-methyl-N-toluene-4-sulfonylamino)ethyl)(CH₃)N-C(O)O-]benzyl,
4-[(2'-(morpholin-4'-yl)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(2'-(hydroxy)ethyl)(CH₃)NC(O)O-]benzyl,
4-[bis(2'-(hydroxy)ethyl)NC(O)O-]benzyl,
4-[(2'-(formyloxy)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(CH₃OC(O)CH₂)HNC(O)O-]benzyl,
4-[2'-(phenylNHC(O)O-)ethyl-]HNC(O)O-]benzyl,
3-chloro-4-[(CH₃)₂NC(O)O-]benzyl,
3-chloro-4-[(4'-methylpiperazin-1'-yl)C(O)O-]benzyl,
3-chloro-4-[(4'-(pyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
3-chloro-4-[(thiomorpholin-4'-yl)C(O)O-]benzyl, and
3-fluoro-4-[(CH₃)₂NC(O)O-]benzyl.

44. A compound according to Claim 35 wherein R⁶ is selected from the group consisting of 2,4-dioxo-tetrahydrofuran-3-yl (3,4-enol), methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *t*-butoxy, cyclopentoxy, cyclopropylmethoxy, neopentoxy, 2- α -isopropyl-4- β -methylcyclohexoxy, 2- β -isopropyl-4- β -methylcyclohexoxy, 2-methoxyphenoxy, 2-(morpholin-4-yl)ethoxy, -O(CH₂CH₂O)₂CH₃, 2-(phenoxy)ethoxy, -OCH₂C(CH₃)₂NHBoc, -NH₂, benzyloxy, -NHCH₂COOH, -NHCH₂CH₂COOH, -NH-adamantyl, -NHSO₂-*p*-CH₃- ϕ , -NHCH₂CH₂COOCH₂CH₃, -NHOY' where Y' is hydrogen, methyl, *iso*-propyl or benzyl, -O-(N-succinimidyl), -O-cholest-5-en-3- β -yl, -OCH₂-OC(O)C(CH₃)₃, -O(CH₂)_zNHC(O)W where *z* is 1 or 2 and W is selected from the group consisting of pyrid-3-yl, N-methylpyridyl, and N-methyl-1,4-dihydro-pyrid-3-yl, -

NR''C(O)-R' where R' is aryl, heteroaryl or heterocyclic and R'' is hydrogen or -
CH₂C(O)OCH₂CH₃.

45. A compound selected from the group consisting of:

N-(toluene-4-sulfonyl)sarcosyl-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine
isopropyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine *tert*-
butyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(*N,N*-dimethylcarbamyloxy)phenylalanine

N-(toluene-4-sulfonyl)sarcosyl-L-4-(morpholin-4-ylcarbonyloxy)phenylalanine *tert*-
butyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(isonipecotoxyloxy)phenylalanine

N-(toluene-4-sulfonyl)sarcosyl-L-4-(4-methylpiperazin-1-
ylcarbonyloxy)phenylalanine *tert*-butyl ester

N-(toluene-4-sulfonyl)-L-*N*-methylalanyl-L-4-(4-methylpiperazin-1-
ylcarbonyloxy)phenylalanine *tert*-butyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(thiomorpholin-4-ylcarbonyloxy)phenylalanine
tert-butyl ester

N-(toluene-4-sulfonyl)-L-*N*-methylalanyl-L-4-(4-methylpiperazin-1-
ylcarbonyloxy)phenylalanine

N-(toluene-4-sulfonyl)sarcosyl-L-4-(1,1-dioxothiomorpholin-4-
ylcarbonyloxy)phenylalanine *tert*-butyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(thiomorpholin-4-ylcarbonyloxy)phenylalanine

N-(toluene-4-sulfonyl)-L-*N*-methylalanyl-L-4-(*N,N*-
dimethylcarbamyloxy)phenylalanine *tert*-butyl ester

N-(toluene-4-sulfonyl)sarcosyl-L-4-(1,1-dioxothiomorpholin-4-
ylcarbonyloxy)phenylalanine

N-(toluene-4-sulfonyl)-*L*-*N*-methylalanyl-*L*-4-(*N,N*-dimethylcarbamoyloxy)phenylalanine

N-(toluene-4-sulfonyl)-*L*-*N*-methyl-2-(*tert*-butyl)glyciny-*L*-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine *tert*-butyl ester

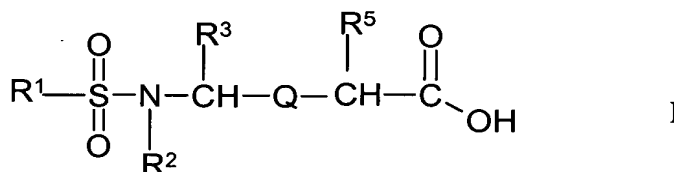
3-[*N*-(toluene-4-sulfonyl)-*N*-methylamino]-1-[1-carboxy-2-(*N,N*-dimethylcarbamoyloxy)phenylethyl]azetidine

N-(toluene-4-sulfonyl)-*L*-prolyl-*L*-4-(isonipecotoxyloxy)phenylalanine *tert*-butyl ester

N-(methanesulfonyl)-*N*-benzylglyciny-*L*-4-(*N,N*-dimethylcarbamoyloxy)phenylalanine *tert*-butyl ester

and pharmaceutically acceptable salts thereof as well as any of the ester compounds recited above wherein one ester is replaced with another ester selected from the group consisting of methyl ester, ethyl ester, *n*-propyl ester, isopropyl ester, *n*-butyl ester, isobutyl ester, *sec*-butyl ester, *tert*-butyl ester and neopentyl ester.

46. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula I:



wherein

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

Q 2
cont R² is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R³ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic;

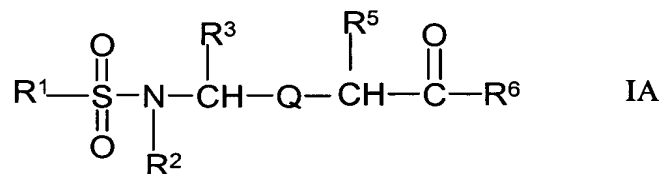
R⁵ is $-(CH_2)_x-Ar-R^{5'}$ where R^{5'} is selected from the group consisting of $-O-Z-NR^8R^{8'}$ and $-O-Z-R^{12}$ wherein R⁸ and R^{8'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R⁸ and R^{8'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of $-C(O)-$ and $-SO_2-$,

Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

x is an integer of from 1 to 4;

Q is $-C(X)NR^7-$ wherein R⁷ is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur; and pharmaceutically acceptable salts thereof.

47. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of formula IA:



wherein

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R^2 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R^3 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic;

R^5 is $-(CH_2)_x-Ar-R^{5'}$ and $R^{5'}$ is selected from the group consisting of $-O-Z-NR^8R^{8'}$ and $-O-Z-R^{12}$ wherein R^8 and $R^{8'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R^8 and $R^{8'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of $-C(O)-$ and $-SO_2-$,

Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

x is an integer of from 1 to 4;

R^6 is selected from the group consisting of amino, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, $-O-(N\text{-succinimidyl})$, $-NH\text{-adamantyl}$, $-O\text{-cholest-5-en-3-}\beta\text{-yl}$, $-NHOY$ where Y is hydrogen, alkyl, substituted alkyl, aryl, and substituted aryl, $-NH(CH_2)_pCOOY$ where p is an integer of from 1 to 8 and Y is as defined above, $-OCH_2NR^9R^{10}$ where R^9 is selected from the group consisting of $-C(O)\text{-aryl}$ and $-C(O)\text{-substituted aryl}$ and R^{10} is selected from the group consisting of hydrogen and $-CH_2COOR^{11}$ where R^{11} is alkyl, and $-NHSO_2Z'$ where Z' is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

Q is $-C(X)NR^7-$ wherein R^7 is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur;

and pharmaceutically acceptable salts thereof.

48. A pharmaceutical composition according to Claims 46 or 47 wherein R¹ is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl.

49. A pharmaceutical composition according to Claims 46 or 47 wherein R¹ is selected from the group consisting of methyl, isopropyl, *n*-butyl, benzyl, phenethyl, phenyl, 4-methylphenyl, 4-*t*-butylphenyl, 2,4,6-trimethylphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2,4-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 3-chloro-4-fluorophenyl, 4-bromophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 4-*t*-butoxyphenyl, 4-(3'-dimethylamino-*n*-propoxy)-phenyl, 2-carboxyphenyl, 2-(methoxycarbonyl)phenyl, 4-(H₂NC(O)-)phenyl, 4-(H₂NC(S)-)phenyl, 4-cyanophenyl, 4-trifluoromethylphenyl, 4-trifluoromethoxyphenyl, 3,5-di-(trifluoromethyl)phenyl, 4-nitrophenyl, 4-aminophenyl, 4-(CH₃C(O)NH-)phenyl, 4-(PhNHC(O)NH-)phenyl, 4-amidinophenyl, 4-methylamidinophenyl, 4-(CH₃SC(=NH)-)phenyl, 4-chloro-3-(H₂NS(O)₂-)phenyl, 1-naphthyl, 2-naphthyl, pyridin-2-yl, pyridin-3-yl, pyrimidin-2-yl, quinolin-8-yl, 2-(trifluoroacetyl)-1,2,3,4-tetrahydroisoquinolin-7-yl, morpholin-4-yl, 2-thienyl, 5-chloro-2-thienyl, 2,5-dichloro-4-thienyl, 1-N-methylimidazol-4-yl, 1-N-methylpyrazol-3-yl, 1-N-methylpyrazol-4-yl, 1-N-butylpyrazol-4-yl, 1-N-methyl-3-methyl-5-chloropyrazol-4-yl, 1-N-methyl-5-methyl-3-chloropyrazol-4-yl, 2-thiazolyl and 5-methyl-1,3,4-thiadiazol-2-yl.

50. A pharmaceutical composition according to Claims 46 or 47 wherein R² is selected from the group consisting of hydrogen, methyl, phenyl, benzyl, -(CH₂)₂-2-thienyl, and -(CH₂)₂- ϕ .

51. A pharmaceutical composition according to Claims 46 or 47 wherein R³ is selected from the group consisting of methyl, phenyl, benzyl, diphenylmethyl, -CH₂CH₂-COOH, -CH₂-COOH, 2-amidoethyl, *iso*-butyl, *t*-butyl, -CH₂O-benzyl and hydroxymethyl.

52. A pharmaceutical composition according to Claims 46 or 47 wherein Q is -C(O)NH- or -C(S)NH-.

53. A pharmaceutical composition according to Claims 46 or 47 wherein Ar is aryl or substituted aryl.

54. A pharmaceutical composition according to Claim 53 wherein Ar is phenyl or substituted phenyl and x is 1.

55. A pharmaceutical composition according to Claim 46 or 47 wherein R⁵ is selected from the group consisting of

- 3-[(CH₃)₂NC(O)O-]benzyl,
- 4-[(CH₃)₂NC(O)O-]benzyl,
- 4-[(CH₃)₂NS(O)₂O-]benzyl,
- 4-[(piperidin-1'-yl)C(O)O-]benzyl,
- 4-[(piperidin-4'-yl)C(O)O-]benzyl,
- 4-[(1'-methylpiperidin-4'-yl)C(O)O-]benzyl,
- 4-[(4'-hydroxypiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(4'-formyloxypiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(4'-ethoxycarbonylpiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(4'-carboxylpiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(3'-hydroxymethylpiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(4'-hydroxymethylpiperidin-1'-yl)C(O)O-]benzyl,
- 4-[(4'-phenyl-1'-Boc-piperidin-4'-yl)-C(O)O-]benzyl,
- 4-[(4'-piperidin-1'-yl ethylene ketal)C(O)O-]benzyl,

09967619 : 111501

2
cont

4-[(piperazin-4'-yl)-C(O)O-]benzyl,
4-[(1'-Boc-piperazin-4'-yl)-C(O)O-]benzyl,
4-[(4'-methylpiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-methylhomopiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(2-hydroxyethyl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-phenylpiperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(4-trifluoromethylpyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyrimidin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-acetyl piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(pyridin-4-ylC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylNHC(O)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-(phenylNHC(S)-)piperazin-1'-yl)C(O)O-]benzyl,
4-[(4'-methanesulfonylpiperazin-1'-yl-C(O)O-)benzyl,
4-[(4'-trifluoromethanesulfonylpiperazin-1'-yl-C(O)O-)benzyl,
4-[(morpholin-4'-yl)C(O)O-]benzyl,
3-nitro-4-[(morpholin-4'-yl)-C(O)O-]benzyl,
4-[(thiomorpholin-4'-yl)C(O)O-]benzyl,
4-[(thiomorpholin-4'-yl sulfone)-C(O)O-]benzyl,
4-[(pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-methylpyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(methoxycarbonyl)pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(hydroxymethyl)pyrrolidin-1'-yl)C(O)O-]benzyl,
4-[(2'-(N,N-dimethylamino)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(2'-(N-methyl-N-toluene-4-sulfonylamino)ethyl)(CH₃)N-C(O)O-]benzyl,
4-[(2'-(morpholin-4'-yl)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(2'-(hydroxy)ethyl)(CH₃)NC(O)O-]benzyl,
4-[bis(2'-(hydroxy)ethyl)NC(O)O-]benzyl,

2
cont

00997619-11504

4-[(2'-(formyloxy)ethyl)(CH₃)NC(O)O-]benzyl,
4-[(CH₃OC(O)CH₂)HNC(O)O-]benzyl,
4-[2'-(phenylNHC(O)O-)ethyl-]HNC(O)O-]benzyl,
3-chloro-4-[(CH₃)₂NC(O)O-]benzyl,
3-chloro-4-[(4'-methylpiperazin-1'-yl)C(O)O-]benzyl,
3-chloro-4-[(4'-(pyridin-2-yl)piperazin-1'-yl)C(O)O-]benzyl,
3-chloro-4-[(thiomorpholin-4'-yl)C(O)O-]benzyl, and
3-fluoro-4-[(CH₃)₂NC(O)O-]benzyl.

56. A pharmaceutical composition according to Claim 47 wherein R⁶ is selected from the group consisting of 2,4-dioxo-tetrahydrofuran-3-yl (3,4-enol), methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, *t*-butoxy, cyclopentoxy, cyclopropylmethoxy, neopentoxy, 2- α -isopropyl-4- β -methylcyclohexoxy, 2- β -isopropyl-4- β -methylcyclohexoxy, 2-methoxyphenoxy, 2-(morpholin-4-yl)ethoxy, -O(CH₂CH₂O)₂CH₃, 2-(phenoxy)ethoxy, -OCH₂C(CH₃)₂NHBoc, -NH₂, benzyloxy, -NHCH₂COOH, -NHCH₂CH₂COOH, -NH-adamantyl, -NHSO₂-*p*-CH₃- ϕ , -NHCH₂CH₂COOCH₂CH₃, -NHOY' where Y' is hydrogen, methyl, *iso*-propyl or benzyl, -O-(N-succinimidyl), -O-cholest-5-en-3- β -yl, -OCH₂-OC(O)C(CH₃)₃, -O(CH₂)_zNHC(O)W where *z* is 1 or 2 and W is selected from the group consisting of pyrid-3-yl, N-methylpyridyl, and N-methyl-1,4-dihydro-pyrid-3-yl, -NR''C(O)-R' where R' is aryl, heteroaryl or heterocyclic and R'' is hydrogen or -CH₂C(O)OCH₂CH₃.

57. A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample with a compound of Claim 1 or 35 under conditions wherein said compound binds to VLA-4.

58. A method for treating an inflammatory condition in a mammalian patient which condition is mediated by VLA-4 which method comprises administering to said

patient a therapeutically effective amount of a pharmaceutical composition of Claim 46 or 47.

59. The method according to Claim 58 wherein said inflammatory condition is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, stroke, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury.

Conclusion

Early examination on the merits is respectfully requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____

Leslie J. Boley

Registration No. 41,490

P.O. Box 1404
Alexandria, Virginia 22313-1404
(650) 622-2300

Date: November 14, 2001